REMARKS

Prosecution

Applicants respectfully request reconsideration of the outstanding rejections and objections in view of the following Remarks.

Claim Amendments

Upon entry of the foregoing amendment, claims 1, 7, 8, 14, and 15-38 are pending in the application. Please cancel claims 2-6 and 9-13 without prejudice or disclaimer to the subject matter therein. Please add claims 33-38. Applicants have amended claims 1 and 8. Support for the claims amendments and the new claims can be found throughout the specification and in the claims as originally filed, for example, at paragraphs [0050], [0071], and [0085], Example 16, and original claims 2 and 7. Applicants respectfully request entry of the above amendment and submit that the above amendment does not constitute new matter.

Specification Amendments

Applicants have added a proper trademark symbol to the Trademarks in the specification identified by the Office Action. Applicants have also added SEQ ID NOs to page 37 to identify HISVNDL as SEQ ID NO: 31 and HLSVNDL as SEQ ID NO: 32. Applicants have also corrected a typographical error. Support for the amendments to the specification can be found throughout the specification and in the claims as originally filed. Applicants respectfully request entry of the above amendment and submit that the above amendment does not constitute new matter.

Information Disclosure Statement

The Office Action stated that EP 967207, submitted in the Information Disclosure Statement filed December 4, 2003, was not considered because it is in a language other than English.

Applicant provides herewith a PTO/SB/08A form listing U.S. Patent No. 6,034,250 which corresponds to EP 967207. Consideration of the foregoing plus the return of a copy of the enclosed Form PTO/SB/08A with the Examiner's initials in the left column in accordance with MPEP § 609 is respectfully requested. Applicants will provide English language documents that

correspond to WO 95/04041, Tatewaki (1992), and Tatewaki (1995) in a subsequent communication.

Sequence Compliance

Applicants have submitted a substitute amendment sequence listing including new SEQ ID NOs for the sequence at page 37, line 1 of the specification. As explained above, Applicants added SEQ ID NOs to page 37 of the specification to identify HISVNDL as SEQ ID NO: 31 and HLSVNDL as SEQ ID NO: 32. Applicants respectfully submit that the instant application is in compliance with the requirements as set forth in 37 C.F.R. §§ 1.821-1.825.

Objection to the Specification

The specification was objected to because of informalities. Applicants have added a proper trademark symbol to indicate the trademarks in the specification. Applicants respectfully submit that "THERMO Sequences" is already identified with a Trademark symbol and does not need to be capitalized. See M.P.E.P. § 608.01(v).

Objection to the Claims

Claims 1 and 2 were objected to because of informalities. Applicants have amended claim 1 and cancelled claim 2 rendering the objection *moot*.

Double Patenting

Claim 7 was objected to under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 1. This double patenting rejection is improper because claim 1 is directed diseases associated with decreased expression of AOP-1 gene or AOP-1 whereas claim 7 further limits claim 1 by specifying the diseases. The USPTO previously acknowledged this in the Restriction Requirement of January 13, 2006, where the USPTO issued a species requirement between the conditions listed in claim 7. Applicants elected chronic heart failure for claim 7 in the Response filed June 13, 2006.

Similarly, claim 14 was objected to under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 8. As discussed above, this double patenting rejection is improper for similar reasons.

It is Applicant's understanding that the Restriction Requirement of January 13, 2006 is still in effect. If this is not the case, Applicants respectfully request clarification of the status of the Restriction Requirement.

Applicants respectfully request reconsideration and withdrawal of this rejection.

Claim Rejections - 35 U.S.C. § 112, first paragraph— written description

Claims 1-14 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention.

As an initial matter, Applicants have amended claims 1 and 8 to recite that the nucleic acid is a nucleic acid encoding AOP-1, or a nucleic acid that hybridizes under stringent conditions to a complementary strand of a nucleic acid encoding AOP-1 and encodes a polypeptide that retains the function of AOP-1. Applicants have also cancelled claims 2-6 and 9-13.

To the extent this rejection applies to the claims as amended, Applicants make the following remarks.

The Office Action states that, "...the specification fails to disclose any nucleic acid encoding a polypeptide having an addition, deletion, or substitution of one or more amino acids as compared with the amino acid sequence of AOP-1 while retaining the function of AOP-1 and fails to disclose any material that enhances AOP-1 expression, production or function other than AOP-1 itself." Office Action at 8.

Applicants traverse this rejection. Applicants submit support for this language in the specification may be found, for example, ¶¶ [0044] and [0085], thus satisfying the written description requirement. Applicants also submit that the nucleic acids taught in the specification include nucleic acids encoding a polypeptide having an addition, deletion, or substitution of one or more amino acids as compared with the amino acid sequence of AOP-1 while retaining the function of AOP-1. The specification provides assays to identify nucleic acids that hybridize under stringent conditions to a complementary strand of a nucleic acid encoding AOP-1 as well as include nucleic acids encoding a polypeptide having an addition, deletion, or substitution of one or more amino acids as compared with the amino acid sequence of AOP-1 which retain the

function of AOP-1 as now claimed. In light of these amendments, Applicants respectfully request reconsideration and withdrawal of the written description rejection.

Claim Rejections - 35 U.S.C. § 112, first paragraph— enablement

Claims 1-14 were rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth at page 10 of the Office Action.

As discussed above, Applicants have amended claims 1 and 8. Claims 2-6 and 9-13 have been cancelled.

To the extent this rejection applies to the claims as amended, Applicants make the following remarks.

Applicants assert that the USPTO has applied the incorrect standard for the test of enablement. In particular, the Office Action requires that the invention be held to a clinical standard, "...at the time of filing, the art of gene therapy for cardiac disease was premature for clinical use and many obstacles would need to be overcome before human trials were possible." Office Action at 12.

The question of enablement, however, is a question of law rather than one of clinical readiness. In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). Indeed, the USPTO may not use clinical standards for enablement. See e.g., In re Brana 51 F.3d 1560, 1568, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995). In In re Brana, the Federal Circuit reversed a USPTO decision based on finding that *in vitro* data did not support *in vivo* applications. Id. at 1566, 1441. Thus, to satisfy the enablement requirement, the specification need only show a nexus between the compound's activity and the disease state being treated.

Applicants assert that the specification provides this required nexus. The specification teaches at least three examples of the practicing the claimed invention in rat models. For example, the specification teaches the protective effect of AOP-1 on the heart in a rat model as acknowledged by the Office Action. See Office Action at 12. Accordingly, Applicants have provided the requisite data to teach one of skill in the art to make and use the claimed invention.

The Office Action also alleges that undue experimentation would be required to treat species other than rodents and cites the 1998 and 2000 Hajjar publications. Contrary to the USPTO assertion, the specification does not cite to or rely on either Hajjar publication. Notably,

in contrast to the USPTO position, Hajjar (1998) teaches that rat models are an appropriate animal model for studying gene transfer. See e.g., Hajjar at page 5256.

Further, the USPTO's reliance on Hajjar (2000) is improper because it is directed to the efficacy and safety which as discussed in In re Brana are the purview of the Food and Drug Administration. See e.g., "[t]he Commissioner, as did the Board, confuses the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption. See Scott v. Finney, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed. Cir. 1994) ('Testing for the full safety and effectiveness of a prosthetic device is more properly left to the Food and Drug Administration (FDA). Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings.')." In re Brana at 1567, 1442.

Finally, concerning the applicability of the invention as a prophylactic or therapeutic method for diseases other than chronic heart failure, the specification teaches several different disease models. For instance, Example 10 teaches a nephritis model, a septic shock (infectious hepatitis) model, and a brain damage model. Example 13 teaches a glutamate toxicity assay, a model for Parkinson's disease. Examples 17 and 18 demonstrates the protective effect of AOP-1 on the brain and kidney, respectively. Accordingly, one of skill in the art can practice the full scope of the claimed invention in view of the specification.

Claim Rejections - 35 U.S.C. § 112, second paragraph

Claims 1-7 and 9-13 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards at the invention.

Applicants have amended claim 1 and cancelled claims 2-7 and 9-13 rendering this rejection *moot*.

Claim Rejections - 35 U.S.C. § 102

Claims 1 and 3-14 were rejected under 35 U.S.C. § 102(b) as being anticipated by Tsuji *et al.* (1995) "Mammalian antioxidant protein complements alkylhydroperoxide reductase (ahpC) mutation in *Escherichia coli*." Biochem. J. 307(2): 377-81.

Applicants have amended claim 1 and cancelled claims 3-7 and 9-13 rendering this rejection *moot*.

CONCLUSION

Applicants respectfully submit that claims are in condition for allowance, and such disposition is earnestly solicited. Should the Examiner believe that any issues remain after consideration of this Response, the Examiner is invited to contact the Applicants' undersigned representative to discuss and resolve such issues.

Respectfully submitted,

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Dated: February 9, 2007 By: _____

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